

REMARKS

By the foregoing amendments, pages 20-22 of the specification have been amended. Also, claim 110 has been amended, and claims 114 and 115 have been added. Support for the amendments to claim 110 can be found in the specification at page 7, line 23 to page 9, line 34, and page 11, line 17 to page 15, line 2; and support for new claims 114 and 115 can be found at page 12, line 26 to page 13, line 5, and page 14, lines 5-6. Claims 110-115 are pending in the application.

The Informalities

The Examiner has noted several instances on pages 20-22 where clarification or correction is required. The enclosed replacement pages are believed to address all of those issues raised by the Examiner. The Examiner also mentioned that he was including annotated pages 20 and 21 with additional guidance. We have not received those annotated pages. If the enclosed replacement pages are still insufficient, Applicants request that the Examiner so advise.

The Rejection under 35 USC § 112, First Paragraph

Claim 110 stands rejected under Section 112, first paragraph, as insufficiently described and/or enabled by the specification. Specifically, the Examiner objects to the presence of "halogen" in the Markush group of Nu's. Solely in the interest of expediting prosecution, Applicants have amended claim 110 to cancel the recitation of halogen. Applicants have also deleted -O-Alk from the Markush group of claim 110.

Claim 110 is objected to because "NH<sub>2</sub>" lacks a hyphen; this has been corrected in the claims listing. Additionally, claim 13 lacks a period; this has also been corrected.

The Rejection under 35 USC § 112, Second Paragraph

Claims 110-113 stand rejected under Section 112, second paragraph, as allegedly indefinite. Specifically, claim 110 is alleged to be indefinite because "AC" and "Ac" are typically used to mean acetyl. In compliance with the Examiner's suggestion, claim 110

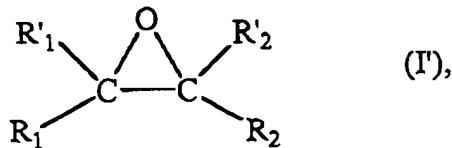
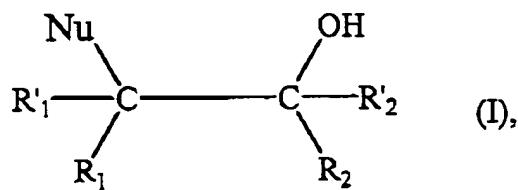
has been amended to replace "AC" and "Ac" with C<sub>1-7</sub> acyl. Likewise, claim 111 has been amended to recite C<sub>1-4</sub> acyl.

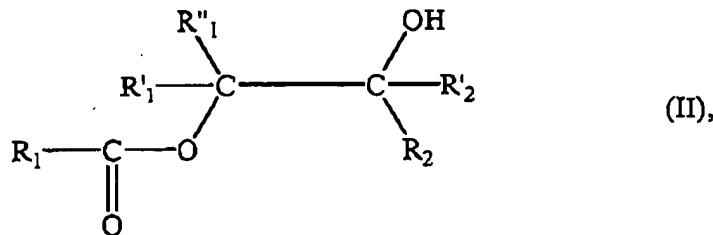
The Rejection under 35 USC § 102(b)

Claims 110-113 stand rejected under Section 102(b) as anticipated over Webb et al., U.S. 4,659,774.

Webb et al., U.S. 4,659,774, describe a polymer-linker for use in oligonucleotide synthesis. In one embodiment, the polymer has oxirane moieties, which are attacked by a linker group with amines at either end. One of the linker group amines serves as the nucleophile to open the oxirane moiety and create a compound in which one of the amines of the linker is covalently attached to a carbon which is adjacent to the carbon with the resulting hydroxy group. The resulting compound is referred to in Webb et al. as a polymer support/linker. This compound is subsequently coupled to a nucleoside by reacting nucleoside-pentachlorophenyl succinate with the polymer support/linker, whereby the free amine of the linker displaces the pentachlorophenyl on the succinate (col. 4, lines 7-15). Thus, the first nucleoside monomer is conjugated to the support via 2 linkers: H<sub>2</sub>N – (CH<sub>2</sub>)<sub>a</sub> – X – (CH<sub>2</sub>)<sub>b</sub> – Y – (CH<sub>2</sub>)<sub>c</sub> – NH<sub>2</sub> and succinate.

In contrast, the subject amended claims are directed to a method of polynucleotide synthesis in which the polymer is one of R<sub>1</sub>, R'<sub>1</sub>, R"<sub>1</sub>, R<sub>2</sub>, and R'<sub>2</sub> in one of the following structures:





The first nucleotide monomer binds via its 3' or 5' phosphate group to, in the case of structures (I) or (II), the OH on the carbon adjacent to the carbon bearing the Nu or acyl group. In the case of structure (I'), the epoxide ring is first opened to generate a hydroxy to which the first monomer becomes attached.

One advantage of the subject method relative to Webb et al. is that at the conclusion of oligonucleotide synthesis in the subject method, the oligonucleotide can be released from the support with a free hydroxy group at its 3' or 5' end in a single deprotection step (page 6, lines 15-22 of the specification). In contrast, Webb et al. involves the use of two linkers, and release of its polynucleotide involves multiple steps of removal from the resin, followed by removal of linker and then detritylation before completely deprotected oligonucleotide is obtained (see Example 4).

The subject method also has the advantage of using the same monomer reagent and reaction conditions for the very first base as for all subsequent bases (page 6, lines 23-29, and page 7, line 32 to page 8, line 1 of the specification). In contrast, the first monomer of Webb is a nucleoside attached to a pentachlorophenyl succinate (col. 4, lines 7-11).

In view of the foregoing distinctive features of the subject method as compared to those of Webb et al., it is submitted that Webb et al. do not anticipate the subject claims. It is also submitted that Webb et al. do not render the amended claims *prima facie* obvious due to the unexpected advantages of a universal support which permits use of the same monomer reagent and reaction conditions for the first base as for all subsequent bases, and at the same time, of a single step to generate a final oligonucleotide with a free 3' or 5' OH group. Design of such a universal support has hitherto been considered as inconceivable due to what was considered to be two conflicting goals (page 6, lines 23-29 of the specification). The subject claims are therefore submitted to be novel and non-

obvious over Webb et al., and withdrawal of the prior art rejection is respectfully requested.

Closing Remarks

It is believed that the foregoing amendments and arguments bring the subject application into condition for allowance and notification of same is respectfully requested.

If the Examiner believes that a phone conference would expedite prosecution, he is respectfully requested to phone the undersigned at 303-268-0066.

Submitted herewith is a check for \$36.00 for the new claims fee. It is believed that no other fees are due with this submission. If this is in error, please charge any necessary fees to Deposit Account No. 19-5117.

Respectfully submitted,

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Enclosures

cc: B. Sauerbrei w/ encls.

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